General

Guideline Title

The role of imaging in the management of adults with diffuse low grade glioma: a systematic review and evidence-based clinical practice guideline.

Bibliographic Source(s)

Fouke SJ, Benzinger T, Gibson D, Ryken TC, Kalkanis SN, Olson JJ. The role of imaging in the management of adults with diffuse low grade glioma: a systematic review and evidence-based clinical practice guideline. J Neurooncol. 2015 Dec;125(3):457-79. [75 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The rating schemes used for the strength of the evidence (Class I-III) and the levels of recommendations (Level I-III) are defined at the end of the "Major Recommendations" field.

Question

What is the optimal imaging technique to be used in the diagnosis of a suspected low grade glioma, specifically: which anatomic imaging sequences are critical for most accurately identifying or diagnosing a low grade glioma and do non-anatomic imaging methods and/or sequences add to the diagnostic specificity of suspected low grade gliomas?

Target Population

These recommendations apply to adults with a newly diagnosed lesion with a suspected or histopathologically proven low grade glioma.

Recommendation

Level II. In patients with a suspected brain tumor, the minimum magnetic resonance imaging (MRI) exam should be an anatomic exam with both T2 weighted and pre- and post-gadolinium contrast enhanced T1 weighted imaging.

Critical Imaging for the Identification and Diagnosis of Low Grade Glioma

Level II. In patients with a suspected brain tumor, anatomic imaging sequences should include T1 and T2 weighted and fluid attenuation inversion recovery (FLAIR) MR sequences and will include T1 weighted imaging after the administration of gadolinium based contrast. Computed

tomography (CT) can provide additional information regarding calcification or hemorrhage, which may narrow the differential diagnosis. At a minimum, these anatomic sequences can help identify a lesion as well as its location, and potential for surgical intervention.

Improvement of Diagnostic Specificity with the Addition of Non-anatomic (Physiologic and Advanced Imaging) to Anatomic Imaging

- *Level II*. Class II evidence from multiple studies and a significant number of Class III series support the addition of diffusion and perfusion weighted MR imaging in the assessment of suspected low grade gliomas, for the purposes of discriminating the potential for tumor subtypes and identification of suspicion of higher grade diagnoses.
- *Level III.* Multiple series offer Class III evidence to support the potential for magnetic resonance spectroscopy (MRS) and nuclear medicine methods including positron emission tomography and single-photon emission computed tomography imaging to offer additional diagnostic specificity although these are less well defined and their roles in clinical practice are still being defined.

Question

Which imaging sequences or parameters best predict the biological behavior or prognosis for patients with low grade glioma?

Target Population

These recommendations apply to adults with a newly diagnosed lesion with a suspected or histopathologically proven low grade glioma.

Recommendation

Anatomic and Advanced Imaging Methods and Prognostic Stratification

Level III. Multiple series suggest a role for anatomic and advanced sequences to suggest prognostic stratification among low grade gliomas. Perfusion weighted imaging, particularly when obtained as a part of diagnostic evaluation (as recommended above) can play a role in consideration of prognosis. Other imaging sequences remain investigational in terms of their role in consideration of tumor prognosis as there is insufficient evidence to support more formal recommendations as to their use at this time.

Question

What is the optimal imaging technique to be used in the follow-up of a suspected (or biopsy proven) low grade glioma?

Target Population

This recommendation applies to adults with a newly diagnosed low grade glioma.

Recommendations

- *Level II*. In patients with a diagnosis of low grade glioma, anatomic imaging sequences should include T2/FLAIR MR sequences and T1 weighted imaging before and after the administration of gadolinium based contrast. Serial imaging should be performed to identify new areas of contrast enhancement or significant change in tumor size, which may signify transformation to a higher grade.
- *Level III*. Advanced imaging utility may depend on tumor subtype. Multicenter clinical trials with larger cohorts are needed. For astrocytic tumors, baseline and longitudinal elevations in tumor perfusion as assessed by dynamic susceptibility contrast perfusion MRI are associated with shorter time to tumor progression, but can be difficult to standardize in clinical practice. For oligodendrogliomas and mixed gliomas, MRS may be helpful for identification of progression.

Definitions

American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Classification of Evidence and Levels of Recommendation on Diagnosis

Class I evidence/Level I (or A) recommendation	Evidence provided by one or more well-designed clinical studies of a *diverse* population using a "gold standard" reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios
Class II evidence/Level II (or B) recommendation	Evidence provided by one or more well-designed clinical studies of a *restricted* population using a "gold standard" reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios

Class III evidence/Level III (or C) recommendation	Evidence provided by expert opinion or studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Diffuse low grade glioma

Guideline Category

Diagnosis

Evaluation

Management

Clinical Specialty

Neurology

Nuclear Medicine

Oncology

Radiology

Intended Users

Physicians

Guideline Objective(s)

- To assess the ability of the most widely used imaging techniques, primarily magnetic resonance imaging (MRI) and positron emission tomography (PET)/radiotracer techniques, to accurately diagnose a low grade glioma (distinguishing this from other tumor types, and from more aggressive primary brain tumors) while simultaneously aiding in the identification of subtypes of tumors for assistance with prognosis and management decisions
- To identify the best imaging sequences for serial longitudinal follow up of suspected or biopsy proven low grade glioma
- To systematically review the evidence available for the imaging of adult patients with low grade glioma
- To make recommendations based on this evidence for the role of imaging in the management of these patients specifically considering the role of imaging in:
    - Diagnostic specificity (distinguishing low grade glioma from higher grade tumors)
    - Prognosis (identifying subtypes of low grade glioma more likely to have an aggressive clinical course)
    - Longitudinal management of patients with low grade glioma

Target Population

- Adults with a newly diagnosed lesion with a suspected or histopathologically proven low grade glioma
- Adults with a newly diagnosed low grade glioma

Interventions and Practices Considered

Magnetic resonance imaging (MRI) techniques

- Anatomic imaging sequences (T2, fluid attenuation inversion recovery [FLAIR], T1 pre- and post contrast, T2*/susceptibility weighted imaging [SWI])
- Perfusion weighted imaging (PWI)
- Diffusion weighted imaging (DWI)/diffusion tensor imaging (DTI)
- Magnetic resonance spectroscopy (MRS)

Nuclear medicine

- [18F]Fluoro-deoxy-glucose (FDG) positron emission tomography (PET)
- [11C]Methionine (MET) PET
- [18F]Fluoro-ethy L-tyrosine (FET) PET
- [201]Thallium single-photon emission computed tomography (SPECT)

Major Outcomes Considered

- Sensitivity, specificity, positive and negative predictive values of diagnostic imaging modalities
- Prognostic value of imaging modalities for tumor growth

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

General Search Strategy

Literature Examination Approach

A wide-ranging literature search strategy was undertaken to identify all citations relevant to the management of low grade gliomas (LGGs). The MEDLINE and EMBASE electronic databases were searched from 1990 through 2012, with additional data being gleaned from the Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Registry, and Cochrane Database of Abstracts of Reviews of Effects. The search strategies used a combination of subheadings and text words with the specifics of this work being outlined in each guideline section. Reference lists of the publications chosen for full text review were also screened for potentially relevant studies.

Study Selection

The search of the bibliographic databases identified possibly relevant citations for a given topic and often these were large in number. The eligibility (inclusion/exclusion) criteria to screen the citations for each of the questions were determined ahead of time for each section by the writing group. At least two authors evaluated the titles and abstracts using the inclusion and exclusion criteria with broad interpretation of the criteria being used initially so as to maximize the likelihood of capturing pertinent information. Cases of disagreement about pertinence were resolved by a third author when needed. The full text articles of the selected abstracts were then collected and the same process of applying the eligibility criteria was carried

out again with the more in depth information available. Articles that met the eligibility criteria were grouped according to the questions they addressed and used to create the evidence tables and scientific foundation sections. Reasons for exclusion for papers were also documented so as to be able to discuss pertinent problem citations in the scientific foundation as needed.

Specific Search Strategy for This Guideline

Literature Review

The following databases were searched from 1990 to 2012 using low-grade glioma and surgery relevant search MeSH and non-MeSH search terms: PubMed (National Library of Medicine, http://www.ncbi.nlm.nih.gov) was searched using Endnote (Thomson Reuters, Inc. http://www.endnote.com) using "ALL FIELDS" and entering "GLIOMA" AND "LOW GRADE" AND "IMAGING" without date limits for a broad initial search. Additional subsequent searches were performed searching "LOW GRADE GLIOMA" and other more specific imaging based terms including "MRI"/"MAGNETIC RESONANCE IMAGING", "CT"/"COMPUTED TOMOGRAPHY", "PET"/"POSITRON EMISSION TOMOGRAPHY", AND "DIFFUSION", "PERFUSION", "SPECTROSCOPY", "FDG", "FET", "MET", AND "SPECT". Potential references were restricted to manuscripts published in the interval between January 1990 and December 2012. The results were then hand searched based on the titles and abstracts to exclude laboratory only studies and titles not on topic. To answer questions related to prognosis, terms of "DIAGNOSIS", "PROGNOSIS", and "NEOPLASM GRADING" were added to the search strategy. Similar search strategies were used to search additional databases including the Cochrane Database of Systematic Reviews, the DARE (Database of Abstracts of Reviews of Effect), and the Cochrane Central Register of Controlled Trials. This overall search strategy yielded a total of 1,297 unique citations.

Article Inclusion and Exclusion Criteria

The 1,297 citations were manually reviewed by the team with specific inclusion and exclusion criteria as outlined below. Four independent reviewers considered abstracted and/or full text data for each article and the two sets of data were compared for agreement by a third party. Inconsistencies were re-reviewed and disagreements were resolved by consensus. Citations that considered adult patients focusing on imaging in the diagnosis, prognostic or longitudinal evaluation of LGG were considered. Manuscripts could focus on a comparison of imaging features of LGG with high grade glioma or other tumor types. Abstracts that focused on a pediatric population, therapeutic studies, case reports noting imaging features of unusual tumor types, articles focusing on brainstem gliomas or spinal cord tumors, or those focusing on imaging and correlative histopathology markers as the primary subject were not included for review. This manual secondary review resulted in a list of 199 references that appeared best suited to answer the questions—those 199 references were pulled for formal paper review and possible inclusion in evidence tables to help answer the key questions.

Number of Source Documents

Overall, 65 publications met the eligibility criteria and are included in the evidentiary tables.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Classification of Evidence and Levels of Recommendation on Diagnosis

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Class III evidence/Level III (or C) recommendation	Evidence provided by expert opinion or studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

General Evidence Analysis

Quality Assessment and Statistical Methods

Articles that met the eligibility criteria were grouped according to the questions they addressed and used to create the evidence tables and scientific foundation sections. Reasons for exclusion for papers were also documented so as to be able to discuss pertinent problem citations in the scientific foundation as needed.

Studies which met the eligibility criteria were subject to more detailed scrutiny and had their data extracted by one reviewer and the extracted information was checked by one or more other reviewers. Evidence and summary tables, reporting the extracted study information and evidence classification, were generated for all of the included studies for each of the questions. Evidence tables were created with most recent data first and subsequent listings in retrograde chronological order. The table headings consisted of first author name and year, followed by a brief study description, chosen data class and conclusion. The authors were directed to craft the data in the tables in a succinct and fact filled manner so as to allow for understanding of the literature entry. The literature in the evidence tables was expanded upon in the scientific foundation of each section so as to emphasize important points supporting its classification and contribution to recommendations. The method by which this was accomplished is expanded upon in the Joint Guideline Committee Guideline Development Methodology document (see the "Availability of Companion Documents" field). Internal drafts of the tables and manuscripts were developed by sharing between writers electronically, by telephone and meetings. Summary and conclusion statements were included for each section, with comments on key issues for future investigation being added where pertinent.

Specific Evidence Analysis for This Guideline

Study Selection and Quality Assessment

Following broad screening for relevance, three independent reviewers evaluated citations and full text screening of potentially relevant papers using a priori criteria for data extraction on a standardized form. Disagreements were resolved with the involvement of a third reviewer, followed by primary re-review until agreement was achieved.

Evidence Classification and Recommendation Levels

Both the quality of the evidence and the eventual strength of the recommendations generated by this evidence were graded according to a three-tiered system for assessing studies addressing diagnostic testing as approved by the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Joint Guidelines Committee on criteria (see the "Rating Scheme for the Strength of the Evidence" field). Imaging studies that considered markers of diagnostic specificity were reviewed using these guidelines, considering a histopathological diagnosis as a "gold standard."

Imaging series that consider these same markers with respect to prognosis were reviewed considering five technical criteria. If all five of these criteria are satisfied, the evidence is classified as Class I. If four out of five are satisfied, the evidence is Class II, and if less than 4 are satisfied, it is Class III (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Guideline Panel Development

Recognizing the serious nature of low grade gliomas along with the lack of consensus among various treatment options, the Joint Tumor Section of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) recommended that evidence-based guidelines be developed as a top priority, for the diagnosis, management and treatment of low grade glioma patients. The objectives of these guidelines are to establish the best evidence-based management of low grade gliomas in terms of imaging diagnosis, use of surgical biopsy and resection, assessment of tumor pathology, administration of systemic chemotherapy, and administration of radiation therapy. Because these tumors dependably recur or progress despite standard therapy, the Joint Tumor Section also recommended an evidence-based guideline be developed for progressive low grade gliomas and that information on promising emerging therapies be assessed in the same manner to determine the possible application of these findings.

Having identified the topical objectives, the Guidelines Committee of the Joint Tumor Section then recruited experts in the field from each of the parent organizations as lead writers of each section. These writers, in turn, recruited experts in non-neurosurgical specialties relevant to the field of management and therapy chosen. Writers were provided training on the method of guideline development as used in this guideline set by written methods and instructions. The senior authors and CNS Guidelines Manager then worked with them on a step by step basis to confirm that the methods were followed as the literature was collected, assessed and documents developed. When writers were approached and preliminarily agreed to participate they were asked to complete a formal conflict of interest questionnaire confirming the appropriateness of their participation. At that point they also agreed to report any new conflicts of interest that might develop during the writing process. In this manner a multidisciplinary panel of writers referred to as the Low Grade Glioma Guidelines Task Force was assembled, with significant administrative, logistical and analytical support from the national CNS Guidelines Committee. The method of this evidence-based clinical practice parameter guideline has been written in a manner to be as transparent as possible using published assessment criteria.

Topic Range of This Systematic Review and Clinical Practice Guideline

Having identified writing groups for each topic, the members designed questions to allow assessment of the literature in a manner that would provide guidance for management of low grade gliomas. These questions are presented at the beginning of each of the eight guideline chapters spanning the topics of imaging assessment, diagnostic biopsy, surgical resection, tumor evaluation by standard neuropathology and molecular techniques, radiation therapy, chemotherapy, emerging therapies and treatment of recurrent or progressive low grade gliomas.

Guideline Panel Consensus

Multidisciplinary writing groups were created for each section based on author expertise, in order to address each of the disciplines and particular areas of therapy selected for these clinical guidelines. Each group was involved with literature selection, creation and editing of the evidence tables and scientific foundations for their specific section and discipline. Using this information, the writing groups then drafted the recommendations in answer to the questions formulated at the beginning of the process, culminating in the clinical practice guideline for their respective discipline. The draft guidelines were then circulated to the entire clinical guideline panel to allow for multidisciplinary feedback, discussion, and ultimately approval.

Rating Scheme for the Strength of the Recommendations

See the "Rating Scheme for the Strength of the Evidence" field.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Approval Process

The completed evidence-based clinical practice guidelines for the management of low grade gliomas were presented to the Joint Guidelines Committee (JGC) of the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) for review. The reviewers for the JGC were vetted by the *Journal of Neuro-oncology* for suitability and expertise to serve as reviewers for the purposes of publication in that journal also. The final product was then approved and endorsed by the executive committees of both the AANS and CNS prior to publication in the *Journal of Neuro-oncology*.

The funding agencies (CNS Executive Committee and AANS/CNS Joint Tumor Section Executive Committee) were permitted to review these guidelines only after the Joint Guidelines Committee had completed its extensive review, critique and ultimate approval process; the funding groups then were limited to whether or not to endorse or reject this body of work but substantive changes were not allowed.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Accurate diagnosis of these tumors (distinction of low grade gliomas from higher grade tumors) and subsequent appropriate management is critically important, and the contribution of imaging to both measures of diagnosis and prognosis is increasingly recognized.
- The advent of magnetic resonance (MR) imaging has not only increased the incidence of early diagnosis of low grade glioma, but also offered additional imaging sequences that could contribute to the non-invasive management of low grade glioma. Nuclear medicine techniques including positron emission tomography (PET) and single-photon emission computed tomography (SPECT) imaging have also been increasingly considered as potential markers for diagnosis and prognostication in low grade glioma.

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

The information in these guidelines reflects the current state of knowledge at the time of completion. Each section is designed to provide an accurate review of the subject matter covered. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Fouke SJ, Benzinger T, Gibson D, Ryken TC, Kalkanis SN, Olson JJ. The role of imaging in the management of adults with diffuse low grade glioma: a systematic review and evidence-based clinical practice guideline. J Neurooncol. 2015 Dec;125(3):457-79. [75 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Dec

Guideline Developer(s)

American Association of Neurological Surgeons - Medical Specialty Society

Congress of Neurological Surgeons - Professional Association

Source(s) of Funding

These guidelines were funded exclusively by the Congress of Neurological Surgeons (CNS) Guidelines Committee, with no funding from any outside commercial sources. Development of this set of evidence-based clinical practice guidelines was editorially independent from the funding agencies.

Guideline Committee

American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Joint Guidelines Committee

Low Grade Glioma Guidelines Task Force

Composition of Group That Authored the Guideline

Authors: Sarah Jost Fouke, Swedish Neuroscience Institute, Seattle, WA, USA; Tammie Benzinger, Washington University School of Medicine, St. Louis, MO, USA; Daniel Gibson, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; Timothy C. Ryken, Department of Neurosurgery, Kansas University Medical Center, Kansas City, KS, USA; Steven N. Kalkanis, Department of Neurosurgery, Henry Ford Health System, Detroit, MI, USA; Jeffrey J. Olson, Department of Neurosurgery, Emory University School of Medicine, Atlanta, GA, USA

Financial Disclosures/Conflicts of Interest

Conflict of Interest

Low Grade Glioma Guidelines Task Force members were required to report all possible conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Joint Guidelines Committee, including potential COIs that are unrelated to the topic of the guideline. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of Task Force Members with possible conflicts and address this by restricting the writing and reviewing privileges of that person to topics unrelated to the possible COIs.

Disclosures

Dr. Kalkanis is a consultant for Arbor and Varian. Dr. Olson is a consultant for the American Cancer Society; has received research funding from the National Cancer Institute, Genentech, and Millennium; and has received investigational drug provision from Merck.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of Neuro-Oncology Web site .

Availability of Companion Documents

The following are available:

- Rock J. Low grade glioma guidelines: foreword. J Neurooncol. 2015 Dec;125(3):447-8. Available from the Journal of Neuro-Oncology Web site .
- Olson JJ, Kalkanis SN, Ryken TC. Evidence-based clinical practice parameter guidelines for the treatment of adults with diffuse low grade glioma: introduction and methods. J Neurooncol. 2015 Dec;125(3):449-56. Available from the Journal of Neuro-Oncology Web site .
- Congress of Neurological Surgeons (CNS). Guideline development methodology: endorsed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the AANS/CNS Joint Guideline Committee. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2012 Feb. 12 p. [2 references]. Available from the Congress of Neurological Surgeons Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 7, 2016. The information was not verified by the guideline developer.

Copyright Statement

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